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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,676	06/08/2000	ANDREA CRISANTI	GJE-39	9050

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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

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DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/486,676

Applicant(s)

CRISANTI, ANDREA

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 25-42 is/are pending in the application.
- 4a) Of the above claim(s) 38, 39 and 42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 25-37, 40, 41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 25-42 are pending. Claims 1-24 are cancelled. Claims 38, 39 and 42 are withdrawn from consideration for being directed to non-elected subject matter. Claims 25-37, 40 and 41 are currently under examination.

This Office Action is in response to the Amendment filed 1/29/03.

#### ***Response to Amendment***

The objection to claims 4-7, 20, 22 and 23 is moot in light of Applicants' cancellation of the claims.

The rejection of claims 8, 9 and 21 under 35 U.S.C.112 2<sup>nd</sup> paragraph is moot in light of Applicants' cancellation of the claims.

The rejection of claims 1, 3 and 19 under 35 U.S.C.102 (b) is moot in light of Applicants' cancellation of the claims.

The rejection of claim 2 under 35 U.S.C.103 (a) is moot in light of Applicants' cancellation of the claims.

Claims 25-37, 40 and 41 are rejected under 35 U.S.C.112 1<sup>st</sup> paragraph (written description) for reasons discussed below.

Claims 25-37, 40 and 41 are rejected under 35 U.S.C.112 1<sup>st</sup> paragraph (scope of enablement) for reasons discussed below.

#### ***Response to Arguments***

##### ***Election/Restrictions***

Applicants request the rejoin of invention of original Groups II and V upon the allowance of composition claims. The restriction requirement was already made final in the Office Action

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(paper No.13) mailed on 10/23/02. No further traversal will be considered. If Applicants do not agree with the restriction requirement, Applicants may petition the Commissioner to review the restriction requirement according to 37 CFR 1.144.

Accordingly, claims 38, 39 and 42 are withdrawn from consideration for being directed to non-elected subject matter. Claims 25-37, 40 and 41 are currently under examination.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-37, 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: “*specification* shall contain a written description of the invention. . . [emphasis added].” The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that “as of the filing date sought, [the inventor] was in possession of the invention.” See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in “possession” of the invention claimed by describing the invention with all of its claimed limitations “by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the

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claimed invention.” See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The claims recite “a functional variant” of the homeodomain of antennapedia (ant). This term encompasses a vast genus polypeptides that comprises any type of variation, including substitution, deletion, insertion or conjugation, to the homeodomain of antennapedia. In analyzing whether the written description requirement is met, it is first determined whether the whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. The specification only discloses a limited number of such functional variants that are known in the art, most of which comprises fragments from the wild type ant homeodomain or with a few point mutations. However, the specification fails to teach which part or what kind of mutations that are responsible for the function of ant homeodomain which include translocation, neurotropic activity and DNA binding. As such, the structural functional relationship is missing. Therefore, the specification fails describe the invention in such a way to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Claims 25-37, 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a conjugate comprising the fusion protein of homeodomain of the ant and a second protein of interest that is at least 100 amino acid in length, and optionally an amino acid tail that binds to an immobilized substrate, wherein the conjugate is not denatured, does not reasonably provide enablement for any conjugate comprising ant

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homeodomain, a second protein that is at least 100 amino acid in length, and other molecules such as nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The nature of the invention is a conjugate comprising the fusion protein of homeodomain of the ant and a second protein of interest that is at least 100 amino acid in length, wherein the ant domain is not denatured. The specification discloses that this conjugate can translocate through cell membrane thus is applicable in methods such as antigen delivery, gene therapy and cancer therapy.

The breath of the claim is broad. The broadest claim encompasses a conjugate of any type comprising an ant homeodomain and a second protein of interest that is at least 100 amino acid in length wherein the ant homeodomain is non-denatured, and wherein the conjugate may comprise other molecules such as nucleic acid.

The teaching of the specification is limited. The specification only discloses a fusion protein comprising a 60 amino acid region of the homeodomain of the ant and full length Mycobacterium tuberculosis antigen 85A. The specification discloses that this fusion conjugate is able to go across cell membrane in non-denatured form. The specification does not disclose a conjugate comprising an ant homeodomain and a protein/nucleic acid complex. The specification also fails to teach how to make such a conjugate.

The state of art at the time of filing does not teach a fusion protein of size more than 100 amino acid linked to ant homeodomain can translocate to cell cytoplasm. The prior art is also silent on whether ant homeodomain can facilitate the translocation of protein/nucleic acid

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complex across cell membrane. Without teaching from the prior art, one skilled in the art would have to rely solely on the teaching of the specification to make and use the invention.

The specification only teaches one example of such a conjugate that is a fusion protein of antigen 85A and ant homeodomain. Although the specification mentioned ant can be linked to protein/nucleic acid complex, it does not teach how to make such conjugate. One may envision that if the second protein is a transcription factor, it would bind corresponding promoter region(s) in which the gene is to be transcribed under non-denaturing condition. However, the specification does not teach a specific utility for such conjugate. The specification also fails to teach whether such protein/nucleic acid complex can be translocate across cell membrane. Whether the claimed conjugate comprising a nucleic acid attached to the second protein can across the cell membrane is unpredictable. Further, the claims recites that only the ant homeodomain is non-denatured, whereas the specification teaches that no translocation is observed when the ant-85A fusion protein is exposed to small amounts of denaturing agent or detergent (see page 26, lines 15-25). As such, whether the claimed conjugate in which the second region is denatured can translocate across cell membrane is unpredictable. Therefore, without teaching from the specification and art, one skilled in the art would have to engage in undue experimentation to make and use the invention in commensurate with the scope of the claims.

### ***Double Patenting***

Applicant is advised that should claim 25 be found allowable, claims 36 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an

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application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.  
April 4, 2003

*Anne-Marie Falk*  
ANNE-MARIE FALK, PH.D.  
PRIMARY EXAMINER